

CAGCGTCAGACGCAGGGCACTGAGAATGTGCGACAGCGCGCAACGATGAAGTAGCCCAGAGGGTCCCTTG
GAAAATGAGGCCAGGGTCCCTGCTGCTGCTTGTCTGCTGCTCGCCCTGTCCAGGAGCCTGCGGGGCAAA
GAGTGTGCGTCTCCACCCTGTGAGTGTACCCAGGAGGACGACTTCAGAGTCACCTGCAAGGAGCTCCACC
GAATCCCCAGCCTGCCGCCAGCACCCAGACTCTGAAGCTCATCGAGACTCATCTGAAGACCATACCCAG
TCTTGCATTTTTCGAGTCTGCCCAATATTTCCAGGATCTATTTATCTATAGATGCAACTCTGCAGCGGCTG
GAACCACATTCTTTCTACAATTTGAGTAAAATGACTCACATAGAAATCCGGAACACCAGAAGCTTAACCT
ATATAGACCCTGATGCCTTGACAGAGCTCCCCCTTGCTCAAGTTTCTTGGCATTTCATACTGGACTTAG
AATATTCCTTGACTTGACCAAAATTTATTCCACGGACATATTCTTTATACTTGAAATCACAGACAACCTT
TACATGACTTCGGTCCCTGAAAACGCATTCCAGGGCCTATGCAATGAAACCTTGACCCTGAAACTGTACA
ACAATGGATTTACTTCAGTCCAAGGACATGCTTTCAATGGAACAAAGCTGGATGCTGTTTACCTAAACAA
GAATAAATACCTGACAGCTATAGACAACGATGCCTTTGGAGGAGTATACAGTGGACCAACTTTGCTAGAT
GTGTCTTCCACCAGCGTCACTGCCCTTCCCTTCCAAAGGCCTGGAGCACCTCAAAGAACTGATCGCAAAAG
ACACCTGGACTCTCAAAAAGCTCCCGCTGTCGTTGAGTTTCCCTCCACCTCACTCGGGCTGACCTCTCTTA
CCCGAGCCACTGCTGCGCTTTTAAGAACCAGAAGAAAATCAGGGGAATCCTGGAGTCTTTGATGTGTAAT
GAGAGCAGTATCCGGAACCTTCGTCAAAGGAAATCAGTGAACATCTTGAGGGGTCCCATCTACCAGGAAT
ATGAAGAAGATCCGGGTGACAACAGTGTTGGGTACAAACAAAACCTCCAAGTTCCAGGAGAGCCCAAGCAA
CTCTCACTATTACGTCTTCTTTGAAGAACAAGAGGATGAGGTCGTTGGTTTCGGCCAAGAGCTCAAAAAT
CCTCAGGAAGAGACTCTCCAAGCCTTCGAGAGCCACTATGACTACACGGTGTGTGGGGACAACGAGGACA
TGGTGTGTACCCCCAAGTCGGACGAGTTTAACCCCTGTGAAGATATCATGGGCTACAGGTTCTTGAGAAT
CGTGGTGTGGTTTGTGAGTCTGCTGGCTCTCCTGGGCAATATCTTCGTCTGCTCATTCTGCTAACCAGC
CACTACAAATTGACCGTGCCGCGGTTCTCATGTGCAACTTGGCCTTTGCAGATTTCTGCATGGGGGTAT
ACCTGCTTCTCATTGCCTCTGTAGACCTGTACACACACTCTGAGTACTACAACCACGCCATCGACTGGCA
GACGGGCCCTGGGTGCAACACGGCTGGCTTCTTCACTGTTTTTCGCCAGTGAGTTATCAGTGTACACACTG
ACGGTCATCACCTGGAGCGATGGTACGCCATCACCTTCGCCATGCGCCTGGATAGGAAGATCCGCCTCA
GGCACGCGTACACCATCATGGCTGGGGGCTGGGTTTCTGCTTCTTCTCGCCCTGCTCCCGATGGTGGG
AATCAGCAGCTATGCCAAGGTCAGCATCTGCCTGCCAATGGACACCGACACCCCTCTTGCACTCGCATAC
ATTGTCCTCGTTCTGCTGCTCAATGTTGTTGCCTTTGTTGTCGTCTGTTCTGCTATGTGAAGATCTACA
TCACGGTCCGAAATCCCCAGTACAACCCTCGAGATAAAGACACCAAGATTGCCAAGAGGATGGCTGTGTT
GATCTTCACTGACTTCATGTGCATGGCGCCCATCTCCTTCTATGCGCTGTCGGCACTTATGAACAAGCCT
CTAATCACTGTTACTAACTCCAAAATCTTGTTGGTTCTCTTCTACCCCTCAACTCCTGTGCCAATCCGT
TTCTCTATGCTATTTTACCAAGGCCTTCCAGAGGGACGTGTTTCATCCTGCTCAGCAAGTTTGGCATCTG
CAAACGCCAGGCCAGGCCTATCAGGGTCAGAGAGTCTGTCCCAACAATAGCACTGGTATTCAGATCCAA
AAGATTCGCCAGGACACGAGGCAGAGTCTCCCAACATGCAAGATACCTATGAACTGCTTGGAAACTCCC
AGCTAGCTCCAAAACCTGCAGGGACAAATCTCAGAAGAGTATAAGCAAACAGCCTTGTAAGGAAAGGCTA
CGCTAGTCACAGTGAGACTTACAAAAGGCTGGTTTCTTGAACATGCGTTCCAGTCCCGTGACATGTGAAC
ACATAGGTTTCATGCAGGTGATGATTCATAGGGTCAGAGTTCATCTCTAGAAAGTATTGCCTC (SEQ ID NO:1)

FIGURE 1A

MRPGSLLLLVLLLALSRLRGKECASPPCECHQEDDFRVTCKELHRIPSLPPSTQTLKLIETHLKTIPSLAFSSLPN
ISRIYLSIDATLQRLPHSFYNLSKMTHEIRNTRSLTYIDPDALTELPLLKFLGIFNTGLRIFPDLTKIYSTDIFF
ILEITDNPYMTSVPENAFQGLCNETLTLKLYNNGFTSVQGHAFNGTKLDAVYLNKNKYLTADNDAFGGVYSGPTLL
DVSSTSVTALPSKGLEHLKELIAKDTWTLKKLPLSLSFLHLTRADLSYPSHCCAFKNQKKIRGILESLMCNESSIRN
LRQRKSVNILRGPIYQEYEEDPGDNSVGKQNSKFQESPSNSHYVFFEEQEDEVVGFGQELKNPQEETLQAFESHY
DYTVCGDNEDMVCTPKSDEFNPCEDIMGYRFLRIVVWFVSLALLGNIFVLLILLTSHYKLTVPFLMCNLAFADFC
MGVYLLLIASVDLYTHSEYYNHAIDWQTGPGCNTAGFFTTFASELSVYTLTVITLERWYAITFAMRLDRKIRLRHAY
TIMAGGWVSCFLLALLPMVGISSYAKVSICLPMDTDTPLALAYIVLVLLLNVAFAVVCSCYVKIYITVRNPQYNPR
DKDTKIAKRMVLIPTDFMCMAPISFYALSALMNKPLITVTNSKILLVLFYPLNSCANPFLYAIFTKAFQRDVFILL
SKFGICKRQAQAYQGQRVCPNNSTGIQIQKIPQDTRQSLPNMQDTYELLGNSQLAPKLQGQISEEYKQTAL (SEQ
ID NO:2)

FIGURE 1B

10045624.102604

underlined = deleted in targeting construct

[] = sequence flanking Neo insert in targeting construct

[CAGCGTCAGACGCAGGGCACTGAGAATGTGCGACAGCGCGCAACGATGAAGTAGCCCAG
AGGGTCCCTTGGAAAATGAGGCCAGGGTCCC] TGCTGCTGCTTGTTCTGCTGCTCGCCCT
GTCCAGGAGCCTGCGGGGCAAAGAGTGTGCGTCTCCACCCTGTGA [GTGTCACCAGGAGG
ACGACTTCAGAGTCACCTGCAAGGAGCTCCACCGAATCCCCAGCCTGCCGCCAGCACCC
AGACTCT] GAAGCTCATCGAGACTCATCTGAAGACCATAACCAGTCTTGCAATTTTCGAGT
CTGCCCAATATTTCCAGGATCTATTTATCTATAGATGCAACTCTGCAGCGGCTGGAACCA
CATTCTTTCTACAATTTGAGTAAAATGACTCACATAGAAATCCGGAACACCAGAAGCTTA
ACCTATATAGACCCTGATGCCTTGACAGAGCTCCCCTTGCTCAAGTTTCTTGGCATTTTC
AATACTGGACTTAGAATATTCCCTGACTTGACCAAAATTTATTCCACGGACATATTCTTT
ATACTTGAAATCACAGACAACCCTTACATGACTTCGGTCCCTGAAAACGCATTCCAGGGC
CTATGCAATGAAACCTTGACCCTGAAACTGTACAACAATGGATTTACTTCAGTCCAAGGA
CATGCTTTCAATGGAACAAAGCTGGATGCTGTTTACCTAAACAAGAATAAATACCTGACA
GCTATAGACAACGATGCCTTTGGAGGAGTATACAGTGGACCAACTTTGCTAGATGTGTCT
TCCACCAGCGTCACTGCCCTTCCTTCCAAAGGCCTGGAGCACCTCAAAGAACTGATCGCA
AAAGACACCTGGACTCTCAAAAAGCTCCCGCTGTGCTTGAGTTTCCTCCACCTCACTCGG
GCTGACCTCTCTTACCCGAGCCACTGCTGCGCTTTTAAGAACCAGAAGAAAATCAGGGGA
ATCCTGGAGTCTTTGATGTGTAATGAGAGCAGTATCCGGAACCTTCGTCAAAGGAAATCA
GTGAACATCTTGAGGGGTCCCATCTACCAGGAATATGAAGAAGATCCGGGTGACAACAGT
GTTGGGTACAAACAAAACCTCCAAGTTCCAGGAGAGCCCAAGCAACTCTCACTATTACGTC
TTCTTTGAAGAACAAGAGGATGAGGTCGTTGGTTTCGGCCAAGAGCTCAAAAATCCTCAG
GAAGAGACTCTCCAAGCCTTCGAGAGCCACTATGACTACACGGTGTGTGGGGACAACGAG
GACATGGTGTGTACCCCCAAGTCGGACGAGTTTAACCCCTGTGAAGATATCATGGGGCTAC
AGGTTCTTGAGAATCGTGGTGTGGTTTGTGCTGCTGCTGGCTCTCCTGGGCAATATCTTC
GTCCTGCTCATTCTGCTAACCAGCCACTACAAATTGACCGTGCCGCGGTTCTCATGTGC
AACTTGCCCTTTGCAGATTTCTGCATGGGGGTATACCTGCTTCTCATTGCCTCTGTAGAC
CTGTACACACACTCTGAGTACTACAACCACGCCATCGACTGGCAGACGGGCCCTGGGTGC
AACACGGCTGGCTTCTTCACTGTTTTTCGCCAGTGAGTTATCAGTGTACACACTGACGGTC
ATCACCTGGAGCGATGGTACGCCATCACCTTCGCCATGCGCCTGGATAGGAAGATCCGC
CTCAGGCACGCGTACACCATCATGGCTGGGGGCTGGGTTTCTTGCTTCTCCTCTCGCCCTG
CTCCCGATGGTGGGAATCAGCAGCTATGCCAAGGTCAGCATCTGCCTGCCAATGGACACC
GACACCCCTCTTGCACTCGCATAATTGTCCTCGTTCTGCTGCTCAATGTTGTTGCCTTT
GTTGTCGTCTGTTCTGCTATGTGAAGATCTACATCACGGTCCGAAATCCCCAGTACAAC
CCTCGAGATAAAGACACCAAGATTGCCAAGAGGATGGCTGTGTTGATCTTCACTGACTTC
ATGTGCATGGCGCCCATCTCCTTCTATGCGCTGTGCGCACTTATGAACAAGCCTCTAATC
ACTGTTACTAACTCCAAAATCTTGTTGGTTCTCTTCTACCCCTCAACTCCTGTGCCAAT
CCGTTTCTCTATGCTATTTTACCAAGGCCTTCAGAGGGACGTGTTTCATCCTGCTCAGC
AAGTTTGGCATCTGCAAACGCCAGGCCAGGCCTATCAGGGTCAGAGAGTCTGTCCCAAC
AATAGCACTGGTATTCAGATCCAAAAGATTCCCCAGGACACGAGGCAGAGTCTCCCAAC
ATGCAAGATACCTATGAACTGCTTGGAACCTCCAGCTAGCTCCAAAACCTGCAGGGACAA
ATCTCAGAAGAGTATAAGCAAACAGCCTTGTAAGGAAAGGCTACGCTAGTCACAGTGAG
ACTTACAAAAGGCTGGTTTCTTGAACATGCGTTCCAGTCCCGTGACATGTGAACACATAG
GTTTCATGCAGGTGATGATTCATAGGGTCAGAGTTCATCTTAGAAAGTATTGCCTC

FIGURE 2A

Gene Sequence Structure
*

91 bp

Sequence Deleted

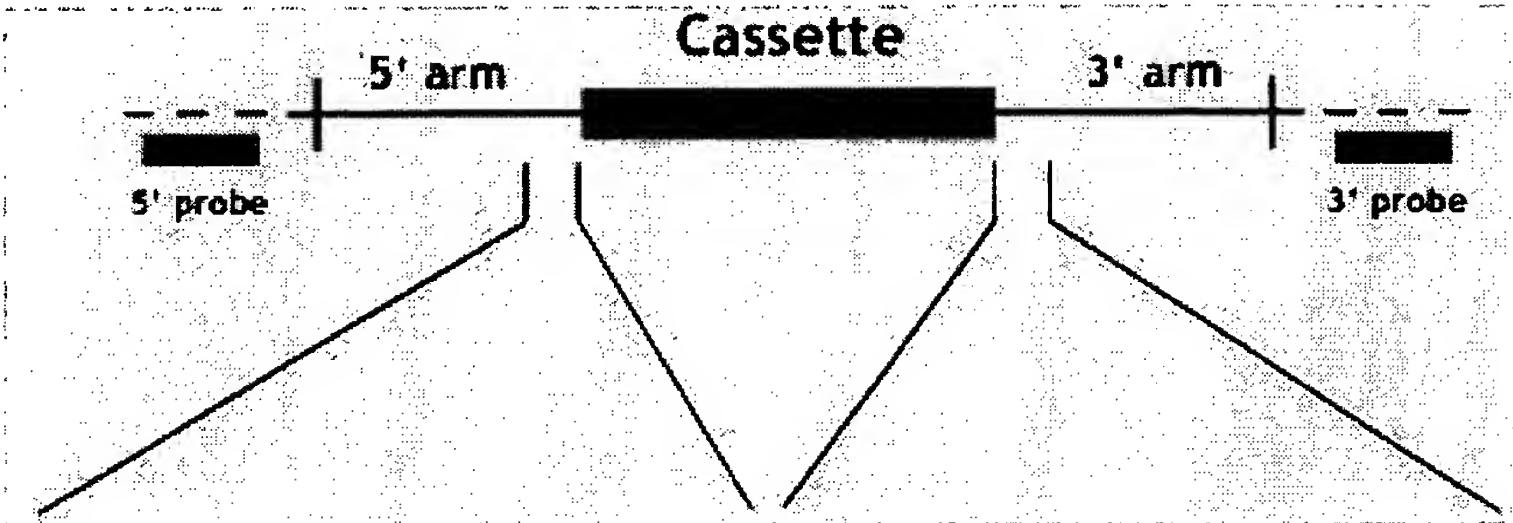
163 bp

Size of full-length
cDNA: 2512 bp



Targeting Vector* (genomic sequence)

LacZ-Neo



Arm Length:
5': 5 kb
3': 1.3 kb

Targeting Vector
Endogenous Locus

* Not drawn to scale

5' >ACTTGAGAGCCTCTCCTTCCC
CCTCTCCAGCGTGCTCTCCAGCGA
TGAGGTCACAGCCCCTCGGAGCCC
TCCTCCTCCCTCCCTTCCCCTCCT
GCACCCGGGTCTCTTCCAGCGTCA
GACGCAGGGCACTGAGAATGTGGC
GACAGCGCGCAACGATGAAGTAGC
CCAGAGGGTCCCTTGAAAATGAG
GCCAGGGTCCC<3'
(SEQ ID NO:3)

5' >GTGTCACCAGGAGGACGACTT
CAGAGTCACCTGCAAGGAGCTCCA
CCGAATCCCCAGCCTGCCGCCAG
CACCCAGACTCTGTGAGTAGCCAA
GGCCAAGACCCCCCCCCCGAGA
AATTCGTGGTGTGTGTTGGGGTGT
GCGCGGATATCTGGTCAGTCCCTG
TACAAATTCAATCCCCCATGCTCG
GGAAGGTCAGC<3'
(SEQ ID NO:4)

FIGURE 2B

Gender	Age (days)	Length (cm)	Body			Spleen/		Liver/		Kidney/		Thymus/		Heart/		Testes + Epididymis Weight (g)
			Weight (g)	Weight (g)	Weight (g)	Weight (g)	Weight (%)	Weight (g)	Weight (%)	Weight (g)	Weight (%)	Weight (g)	Weight (%)	Weight (g)	Weight (%)	
+/-	Female	48	10	22.339	0.095	0.425	1.256	5.622	0.327	1.464	0.082	0.367	0.155	0.694		
+/-	Female	48	8.25	16.960	0.052	0.307	0.900	5.307	0.220	1.297	0.060	0.354	0.122	0.719		
+/-	Male	48	9.5	24.550	0.069	0.281	1.388	5.654	0.342	1.393	0.055	0.224	0.119	0.485		0.224
+/-	Male	48	9.7	23.792	0.081	0.340	1.192	5.010	0.304	1.278	0.063	0.265	0.133	0.559		0.226
-/-	Female	48	8.5	22.619	0.080	0.354	1.272	5.624	0.238	1.052	0.080	0.354	0.121	0.535		
-/-	Male	48	9	24.040	0.072	0.300	1.344	5.591	0.322	1.339	0.062	0.258	0.137	0.570		0.181
-/-	Female	47	7.5	9.026	0.008	0.089	0.435	4.819	0.110	1.219	0.010	0.111	0.045	0.499		
-/-	Female	48	7	8.360	0.016	0.191	0.382	4.569	0.110	1.316	0.004	0.048	0.051	0.610		
-/-	Female	48	8	11.640	0.016	0.137	0.586	5.034	0.127	1.091	0.031	0.266	0.053	0.455		
-/-	Male	48	7.6	11.733	0.018	0.153	0.666	5.676	0.134	1.142	0.034	0.290	0.053	0.452		0.087
-/-	Male	48	8	12.545	0.024	0.191	0.778	6.202	0.146	1.164	0.035	0.279	0.060	0.478		0.180
-/-	Male	48	7	8.070	0.007	0.087	0.366	4.535	0.095	1.177	0.001	0.012	0.042	0.520		0.076

FIGURE 3

Gender	Age at Test (days)	Length (cm)	Body		Spleen/		Liver/		Kidney/		Thymus/		Heart/		Testes + Epididymis	
			Weight (g)	(%)	Weight (g)	(%)	Weight (g)	(%)	Weight (g)	(%)	Weight (g)	(%)	Weight (g)	(%)	Weight (g)	(g)
+/+ Female	308	9.5	25.191	0.222	0.8813	1.476	5.8592	0.353	1.4013	0.039	0.1548	0.145	0.5756			
+/+ Female	308	9.918	28.180	0.091	0.3229	1.447	5.1348	0.383	1.3591	0.043	0.1526	0.136	0.4826			
+/+ Male	308	11.025	55.089	0.182	0.3304	3.267	5.9304	0.694	1.2598	0.074	0.1343	0.219	0.3975	0.35		
+/+ Male	308	11	42.613	0.136	0.3192	2.144	5.0313	0.485	1.1382	0.052	0.1220	0.201	0.4717	0.387		
-/- Female	307	7.978	19.561	0.030	0.1534	0.863	4.4118	0.184	0.9406	0.040	0.2045	0.109	0.5572			
-/- Male	307	9.47	25.557	0.077	0.3013	1.394	5.4545	0.340	1.3304	0.025	0.0978	0.111	0.4343	0.401		
-/- Male	307	9.5	25.263	0.051	0.2019	1.232	4.8767	0.296	1.1717	0.027	0.1069	0.102	0.4038	0.389		

FIGURE 4